

a sea urchin sperm protein, enterokinase and agrin (SEA) domain, and a second EGF domain. The SEA domain contains a putative cleavage site that is conserved in other mucins (Moniaux et al., J. Biol. Chem. 2006). MUC17 is a single-pass transmembrane protein with an 80-amino acid cytoplasmic tail that is intracellular (Moniaux et al., J. Biol. Chem. 2006). The expression of MUC17 in healthy adults is restricted to the apical surface of enterocytes, or mature absorptive epithelial cells, that line the intestine (Moniaux et al., J. Biol. Chem. 2006; Johanasson and Hansson, Nat. Rev. Immunology 2016). MUC17 is also expressed by the stomach and pancreas (Moniaux et al., J. Biol. Chem. 2006; Moehle et al., J. Mol. Med. 2006). The biological function of MUC17 is considered to be the maintenance of mucosal barrier integrity in the intestinal tract, such as by mucosal restitution (Luu et al., Int. J. Biochem. Cell Biol. 2010; Resta-Lenert et al., Am. J. Physiology 2011; Johanasson and Hansson, Nat. Rev. Immunology 2016).

[9] MUC17 is aberrantly expressed in some cancers. MUC17 mRNA was shown to be expressed in one pancreatic cancer cell line and three colon cancer cell lines (Gum et al. 2002). Immunohistochemistry studies confirmed expression of the MUC17 protein in pancreatic cancer ((Moniaux et al. 2006). In colon cancer, however, MUC17 protein expression was shown to be decreased (Senapati et al., J. Clin. Pathol. 2010). Nevertheless, the expression patterns of MUC17 make it a potential target for the treatment of different forms of malignancy.

SUMMARY

[10] In view of the conflicting implications in the literature with regard to MUC17 as a potential target for which pathological condition, it is the object of the present disclosure to clearly identify specific conditions associated with MUC17 upregulation and to provide bispecific antibody constructs, such as T cell engaging molecules, which are specifically suitable to bind MUC17 in a MUC17-associated condition, preferably for use in the treatment of said specific conditions. Accordingly, the present disclosure provides an antibody construct characterized by comprising a first domain binding to MUC17, a second domain binding to an extracellular epitope of the human and non-human, e.g. *Macaca* CD3ε chain, and preferably a third domain, which is a specific Fc modality. Moreover, the disclosure provides a polynucleotide encoding the antibody construct, a vector comprising this polynucleotide, and host cells expressing the construct and a pharmaceutical composition comprising the same.

[11] In one example, it is envisaged in the context of the present disclosure to provide an antibody construct comprising:

- a first domain which binds to MUC17 and
- a second domain which binds to an extracellular epitope of the human and the *Macaca* CD3ε chain.

[11a] In one aspect, the present disclosure refers to a bispecific antibody construct comprising:

- a first domain which binds to MUC17, and
- a second domain which binds to an extracellular epitope of the human and the *Macaca* CD3ε chain, wherein the antibody construct comprises a sequence selected from an amino acid sequence as depicted in any of SEQ ID NOs: 63, 184, or 426.

[12] Within said example, it is further envisaged in the context of the present disclosure that the antibody construct comprises a third domain which comprises two polypeptide monomers, each comprising a

Claims

1. A bispecific antibody construct comprising:
 - a first domain which binds to MUC17, and
 - a second domain which binds to an extracellular epitope of the human and the *Macaca* CD3ε chain, wherein the antibody construct comprises a sequence selected from an amino acid sequence as depicted in any of SEQ ID NOs: 63, 184, or 426.
2. The bispecific antibody construct according to claim 1, having an amino acid sequence selected from the group consisting of:

SEQ ID NOs: 64, 65, 185, 186, 427 and 428, or having an amino acid having at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identity to said sequences.
3. A polynucleotide encoding an antibody construct as defined in any one of claims 1 and 2.
4. A vector comprising a polynucleotide as defined in claim 3.
5. A host cell transformed or transfected with the polynucleotide as defined in claim 3 or with the vector as defined in claim 4.
6. A process for the production of the bispecific antibody construct according to claims 1 and 2, said process comprising culturing a host cell as defined in claim 5 under conditions allowing the expression of the antibody construct as defined in any one of claims 1 and 2 and recovering the produced antibody construct from the culture.
7. A pharmaceutical composition comprising the bispecific antibody construct according to any one of claims 1 and 2 or produced according to the process of claim 6.
8. The pharmaceutical composition of claim 7, which is stable for at least four weeks at about -20°C.

9. The bispecific antibody construct according to any one of claims 1 and 2 or produced according to the process of claim 6, for use in therapy.
10. Use of the bispecific antibody construct according to any one of claims 1 and 2 or produced according to the process of claim 6 in the manufacture of a medicament for the treatment of gastrointestinal cancer or pancreatic cancer, preferably gastric cancer.
11. A kit comprising the bispecific antibody construct according to any one of claims 1 and 2 produced according to the process of claim 6, a polynucleotide as defined in claim 3, a vector as defined in claim 4, and/or a host cell as defined in claim 5.
12. Use of a bispecific antibody construct directed against MUC17 and CD3 and as defined in any one of claims 1 and 2 in the manufacture of a medicament for the treatment or amelioration of gastrointestinal cancer.